

## CLAIMS

1. A method for regulating expression of a *tet* operator-linked gene in a cell of a subject, comprising:
  - 5 introducing into the cell a nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells; and
  - modulating the concentration of a tetracycline, or analogue thereof, in the subject.
- 10 2. The method of claim 1, wherein the Tet repressor of the tTA is a Tn10-derived Tet repressor.
3. The method of claim 1, wherein the polypeptide of the tTA which directly or indirectly activates transcription in eucaryotic cells is from herpes simplex virus virion  
15 protein 16.
4. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is integrated randomly in a chromosome of the cell.
- 20 5. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is integrated at a predetermined location within a chromosome of the cell.
6. The method of claim 1, wherein the nucleic acid molecule encoding the tTA is introduced into the cell *ex vivo*, the method further comprising administering the cell to the  
25 subject.
7. The method of claim 1, wherein the *tet* operator-linked gene is an endogenous gene of the cell which has been operatively linked to the at least one *tet* operator sequence.
- 30 8. The method of claim 1, wherein the *tet* operator-linked gene is an exogenous gene which has been introduced into the cells.
9. The method of claim 1, wherein the tetracycline analogue is anhydrotetracycline, doxycycline or cyanotetracycline.
- 35 10. A method for regulating expression of a gene in a cell of a subject, comprising:
  - obtaining the cell from the subject;
  - introducing into the cell a first nucleic acid molecule which operatively links a gene to at least one *tet* operator sequence;

introducing into the cell a second nucleic acid molecule encoding a tetracycline-controllable transactivator (tTA), the tTA comprising a Tet repressor operably linked to a polypeptide which directly or indirectly activates transcription in eucaryotic cells, to form a modified cell;

5 administering the modified cell to the subject; and  
modulating the concentration of a tetracycline, or analogue thereof, in the subject.

11. The method of claim 10, wherein the Tet repressor of the tTA is a Tn10-derived Tet repressor.

10 12. The method of claim 10, wherein the polypeptide of the tTA which directly or indirectly activates transcription in eucaryotic cells is from herpes simplex virus virion protein 16.

15 13. The method of claim 10, wherein the nucleic acid molecule encoding the tTA is integrated randomly in a chromosome of the cell.

14. The method of claim 10, wherein the nucleic acid molecule encoding the tTA is integrated by homologous recombination at a predetermined location within a chromosome  
20 of the cell.

15. The method of claim 10, wherein the first nucleic acid molecule operatively links an endogenous gene of the cell to at least one *tet* operator sequence.

25 16. The method of claim 10, wherein the first nucleic acid molecule comprises a gene operatively linked to at least one *tet* operator sequence.

17. The method of claim 10, wherein the tetracycline analogue is anhydrotetracycline, doxycycline or cyanotetracycline.